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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/036,724	03/06/1998	SALDONO FERRONE	FER-1	6300

7590 02/19/2004

IMCLONE SYSTEMS INCORPORATED
THOMAS C GALLAGHER
180 VARICK STREET
7TH FLOOR
NEW YORK, NY 10014

EXAMINER	
NICKOL, GARY B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/036,724	FERRONE ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-12,17,18 and 20* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-10,17,18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Ferrone *et al.*

Date of Priority: March 6, 1998

Request for Continued Examination

The request filed on 12-24-03 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/036,724 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 1-2, 6-12, 17-18, and 20 are pending.

Claims 11-12 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1-2, 6-10, 17-18, and 20 are currently under consideration.

Election/Restrictions

Claims 2 and 20 are considered generic to a plurality of disclosed patentably distinct species comprising the following:

1) tumor growth, arthritis, macular degeneration, psoriasis (Claim 2)

2) FLK-1, KDR, FLT-1, TIE-1, or TIE-2/Tek (Claim 20)

The above species encompass distinct diseases which differ at least in etiology, pathology, and mechanisms. Further, the products of the above species represent separate and distinct molecules with different structures and functions such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues.

During a telephone conversation with Kathryn Lumb on February 17, 2004 a provisional election to each species was made. Applicants elected the species of "tumor growth" in Claim 2 and "KDR" in Claim 20. Affirmation of this election must be made by applicant in replying to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 6-10, 17-18, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting an unwanted angiogenic condition in a mammal in need thereof comprising administering to the mammal an effective amount of dendritic cells pulsed with a fusion protein comprising Flk-1 and alkaline phosphatase (Flk-1AP), does not reasonably provide enablement for the broadly claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the

predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method of inhibiting an unwanted angiogenic condition in a mammal in need thereof comprising administering to the mammal an effective amount of a modified immunogen that causes an immune response against a molecule that induces angiogenesis in the mammal, wherein the immunogen comprises an angiogenesis associated receptor.

This includes administering any and all immunogens comprising an angiogenesis associated receptor.

The specification teaches (page 9, line 2) that the immunogens of the invention unexpectedly induce an effective immune response when properly presented to the immune system wherein the immune system preferably inhibits or eliminates the pathological condition associated with angiogenesis, such as growth of cancer cells. The specification teaches (page 9, 2nd paragraph) that the immunogens of the invention may be any angiogenic molecule associated with the process of angiogenesis. The specification further teaches (page 14, 1st paragraph) that "an immune response means production of antibodies, i.e. humoral, and/or a cell-mediated response, such as a T-cell response including helper and cytotoxic T cell responses".

However, one cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to administering any and all angiogenic-associated receptors (including FLK-1, KDR, FLT-1, TIE-1, or TIE-2/Tek) with or without the biological properties representative of what is claimed, and applicant has not enabled the administration of all of these types of modified immunogens because it has not been shown that these modified

immunogens would predictably inhibit angiogenesis by stimulating an immune response. In filing the request for continued prosecution, Applicants submitted a declaration under 37 CFR 1.132 (response filed 12-24-03) by Inventor Hicklin which demonstrated the inhibition of tumor metastases in mice vaccinated with dendritic cells pulsed with the fused immunogen comprising Flk-1 and alkaline phosphatase (Flk-1/AP). However, immunization with pulsed dendritic cells expressing the fused polypeptide does not bear a reasonable correlation to the scope of the claimed invention which is broadly drawn to administering any modified immunogen comprising an angiogenesis associated receptor.

Those of skill in the art recognize that the state of the art of treating cancers by active immunotherapy is highly unpredictable. As set forth previously (Action mailed 10/19/2001), Bellone *et al.* . (Immunology Today, v20 (10), 1999, pp.457-462) summarize the current state of the art of peptide immunotherapy including clinical trials where "there is usually a poor correlation between induction of specific T-cells and the clinical responses" (page 457, 2nd column). Bellone *et al.* teach the disadvantages of peptide cancer immunotherapy in that (1) there is no direct evidence for a role in tumor rejection, (2) the therapy is applicable to few patients, (3) risk of generating tumor escape mutants, and (4) risk of autoimmune reactions (page 461, Box 1). Furthermore, with regards to inhibiting angiogenesis in a human mammal that has cancer, the state of the art is highly unpredictable. For example, it was recently revealed that the drug Endostatin is unlikely to be the kind of across-the-board cancer cure that many had hoped for. Out of the 61 terminally ill patients tested, not one recovery had been seen (MSNBC News Services, "Mixed results on new cancer drug", November 9, 2000).

Thus, only a method of a method of inhibiting an unwanted angiogenic condition in a mammal in need thereof comprising administering to the mammal an effective amount of dendritic cells pulsed with a fusion protein comprising Flk-1 and alkaline phosphatase (Flk-1AP), but not the full scope of the claimed invention meets the scope of enablement requirements under 35 USC 112, 1st paragraph. Accordingly, the disclosure and Inventor's declaration, does not contain sufficient information to enable one skilled in the pertinent to make and use the invention as broadly claimed.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Examiner
Art Unit 1642

GBN